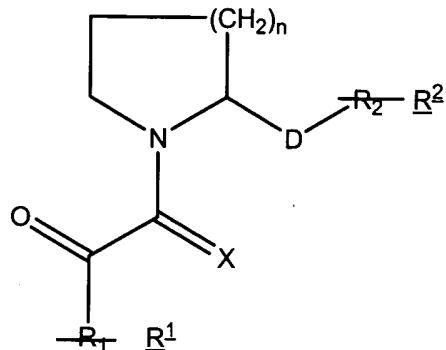


In the Claims:

In accordance with the Pre-OG Notice dated January 31, 2003 permitting amendments in a revised format, applicants provide the following listing of claims.

Claim 1 (currently amended): A compound ~~having the formula (I): of formula~~



or a pharmaceutically acceptable salt, ester, or solvate of the compound, wherein:

*R1*  
Cont.  
n is 1-3;

X is either O or S;

~~R<sub>1</sub> R<sup>1</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;~~

D is a bond, ~~or a~~ C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

~~R<sub>2</sub> R<sup>2</sup> is a carboxylic acid or a carboxylic acid isostere;~~

~~and wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, or carboxylic acid isostere is optionally substituted with one or more substituents selected from R<sub>3</sub> R<sup>3</sup> and Z, where;~~

~~R<sub>3</sub> R<sup>3</sup> and Z are independently hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulfhydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight~~

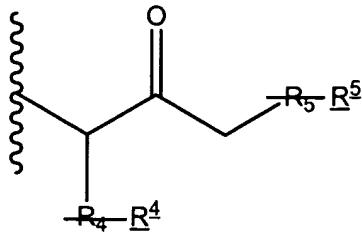
or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, or CO<sub>2</sub>R<sup>7</sup>;

where R<sup>7</sup> is hydrogen, or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl;

~~or a pharmaceutically acceptable salt, ester, or solvate thereof;~~

provided that : when n=1, and D is a bond , and R<sub>2</sub> R<sup>2</sup> is COOH, then R<sub>1</sub> R<sup>1</sup> is not C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, phenylamine, 2-(3, 4-dichlorophenyl)ethyl, hydroxy, ethoxy, benzyl, or Ar+ Ar<sup>1</sup>, wherein Ar+ Ar<sup>1</sup> is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 1-pyridyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, and wherein said alkyl, alkenyl, cycloalkyl, cycloalkenyl, or Ar+ Ar<sup>1</sup> are is optionally substituted with one or more substituents selected from the group consisting of hydrogen, halo, hydroxyl, nitro, trifluoromethyl, C<sub>1</sub>-C<sub>9</sub> straight or branched alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched alkenyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>2</sub>-C<sub>4</sub> alkenyloxy, phenoxy, benzyloxy, COOH, and amino;

further provided that : when n=1, and D is a bond, and R<sub>2</sub> R<sup>2</sup> is the carboxylic acid isostere -CONZ(R<sup>3</sup>), and Z is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl, and R<sup>3</sup> is phenyl, or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkyl or alkenyl, wherein said alkyl is unsubstituted or substituted in one or more positions with Ar<sub>2</sub> Ar<sup>2</sup> as defined below, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, cycloalkyl connected by methyl or a C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkyl or alkenyl chain, C<sub>1</sub>-C<sub>4</sub> alkyl ester, or Ar<sub>3</sub> Ar<sup>3</sup> wherein Ar<sub>3</sub> Ar<sup>3</sup> is selected from the group consisting of 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thiazolyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched alkenyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>2</sub>-C<sub>4</sub> alkenyloxy, phenoxy, benzyloxy, and amino; wherein said alkyl ester is optionally substituted with phenyl; or R<sup>3</sup> is the fragment:



*R<sup>1</sup>*  
*OPM*

wherein R<sub>4</sub> R<sup>4</sup> is selected from the group consisting of straight or branched chain C<sub>1</sub>-C<sub>8</sub> alkyl optionally substituted with C<sub>3</sub>-C<sub>8</sub> cycloalkyl, benzyl, or Ar<sub>2</sub> Ar<sup>2</sup> as defined below, and wherein R<sub>2</sub> R<sup>2</sup> is COOZ or CONR<sup>6</sup>, wherein R<sup>6</sup> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl, and C<sub>2</sub>-C<sub>6</sub> straight or branched alkenyl, and wherein R<sub>5</sub> is selected from the group consisting of phenyl, benzyl, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl, and C<sub>2</sub>-C<sub>6</sub> straight or branched alkenyl, wherein said alkyl or alkenyl is optionally substituted with phenyl; then R<sub>1</sub> R<sup>1</sup> is not C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, substituted thiophene, or C<sub>1</sub>-C<sub>4</sub> alkoxy, wherein said alkyl or alkenyl is optionally substituted in one or more positions with C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, or Ar<sub>2</sub> Ar<sup>2</sup> as , where Ar<sub>2</sub> is defined below, wherein said alkyl, alkenyl, cycloalkyl or cycloalkenyl groups may be is optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> C<sub>2</sub>-C<sub>4</sub> alkenyl, or hydroxy, and wherein Ar<sub>2</sub> Ar<sup>2</sup> is 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, or phenyl, having one to three substituents selected from the group consisting of hydrogen, halo, hydroxy, nitro, trifluoromethyl, C<sub>1</sub>-C<sub>6</sub> straight or branched alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched alkenyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>2</sub>-C<sub>4</sub> alkenyloxy, phenoxy, benzyloxy, and amino;

further provided that : when n=1, and X is O, and D is a bond, and R<sub>2</sub> R<sup>2</sup> is -CONH<sub>2</sub>, then R<sub>1</sub> R<sup>1</sup> is not methyl, ethyl, iso-propyl, iso-butyl, iso-pentyl, 4-methylpentyl, indolyl, phenyl, or hydroxyphenyl;

further provided that : when n=1, and X is O, and D is a bond, and R<sub>2</sub> R<sup>2</sup> is cyano, then R<sub>1</sub> R<sup>1</sup> is not methyl;

~~further provided that:~~

~~when n = 2, and X is O, and D is a bond, and R<sub>2</sub> is CONZ(R<sup>3</sup>), and R<sub>1</sub> is ethoxy, then R<sup>3</sup> or Z is not halo-substituted phenyl;~~

~~further provided that:~~

~~when n = 2, and X is O, and D is a bond, and R<sub>2</sub> is CONZ(R<sup>3</sup>) and R<sub>1</sub> is substituted thiophene or tetrahydropyranoxy, or methoxy, then R<sup>3</sup> or Z is not C<sub>1</sub>-C<sub>4</sub> alkyl ester substituted ethyl;~~

~~further provided that:~~

~~when n = 2, and X is O, and D is a bond, and R<sub>2</sub> is CONZ(R<sup>3</sup>) and R<sub>1</sub> is ethoxy, then R<sup>3</sup> or Z is not 4-chlorophenyl;~~

~~further provided that:~~

~~when n = 2, and X is O, and D is a bond, and R<sub>2</sub> is CONZ(R<sup>3</sup>) and R<sub>1</sub> is cyclohexyl, then R<sup>3</sup> or Z is not ethyl or propyl substituted with phenyl;~~

    further provided that : when D is CH<sub>2</sub>, then R<sub>2</sub> R<sup>2</sup> is not -OMe, -NHMe, or substituted -NHcyclohexyl; and

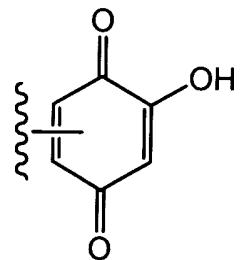
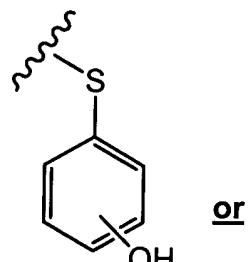
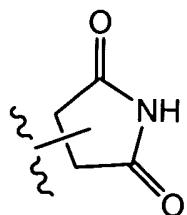
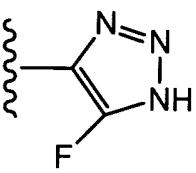
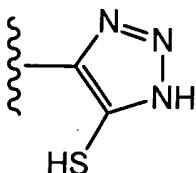
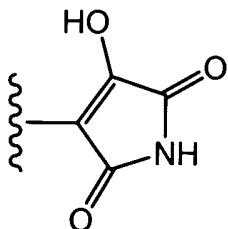
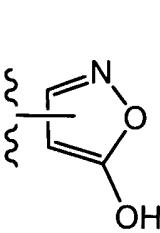
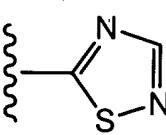
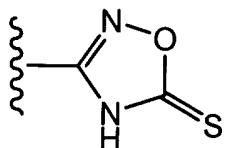
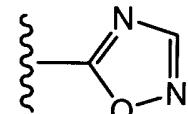
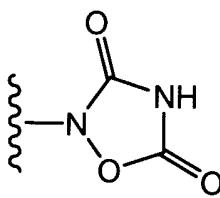
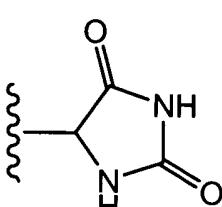
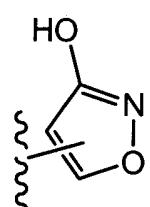
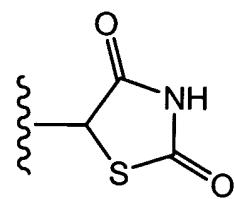
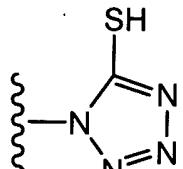
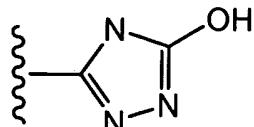
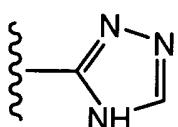
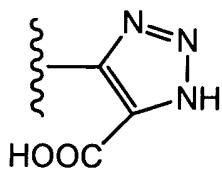
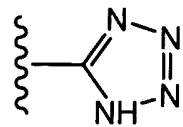
        further provided that : when D is CH<sub>2</sub>, and R<sub>2</sub> R<sup>2</sup> is -OH, then R<sub>1</sub> R<sup>1</sup> is not phenyl or pyrrolidinemethanol ;

~~further provided that:~~

~~when n = 2, and X is O, and D is a bond, and R<sub>2</sub> is COOH, then R<sub>1</sub> is not methyl, tert-butyl, 1,1-dimethyl-2-methyl-propyl, 1,1-dimethyl-propyl, methoxy, ethoxy, phenyl, tetrahydropyranoxy substituted C<sub>4</sub>-C<sub>6</sub> alkyl, 1-methyl-1-methoxyamide, 1-methylcyclohexyl, 3-iodophenyl, 3-methyl-ester-cyclopentyl, 1,1-dimethyl-6-phenylhex-3,5-di oxy, or trimethoxyphenyl.~~

Claim 2 (currently amended): The compound of claim 1, wherein R<sub>2</sub> R<sup>2</sup> is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are is optionally substituted in one or more positions with R<sup>3</sup>.

Claim 3 (currently amended): The compound of claim 1, wherein  $\text{R}_2 \text{ R}^2$  is selected from the group consisting of:



or

*B1  
cont.*

B, wherein the atoms of said ring structure ~~may be~~ is optionally substituted at one or more positions with R<sup>3</sup>.  
cont.

Claim 4 (canceled)

R2 Claim 5 (currently amended): The compounds, (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-hydroxymethylpyrrolidine; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinetetrazole; (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-pyrrolidinecarbonitrile; ~~and (2S)-1-(1,2-dioxo-3,3-dimethylpentyl)-2-aminocarbonyl piperidine;~~ and compounds ~~1-25, 27, 28, 31-33, and 35-136~~ 1, 3, 5, 8, 11, 14, 17, 21, 24-32, 34, 38-40, 44, 45, 47-52, 62, 64-68, 73-98, 101, 102, 106, 108-117 and 119-137 of Tables I, II, and III.

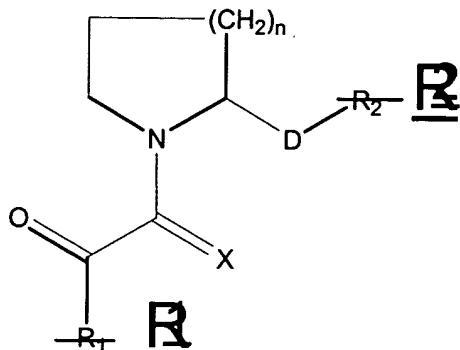
Claim 6 (original): The compound 1-[2-[3-(4-Fluorophenyl)(1,2,4-oxadiazol-5-yl)]pyrrolidinyl]-3,3-di-methylpentane-1,2-dione.

Claim 7 (original): The compound 3,3-Dimethyl-1-[2-(3-methyl(1,2,4-oxadiazol-5-yl))pyrrolidinyl]pentane-1, 2-dione.

Claim 8 (canceled)

B3 Claim 9 (currently amended): ~~The pharmaceutical composition of claim 8, wherein the N-heterocyclic carboxylic acid or carboxylic acid isostere comprises A pharmaceutical composition comprising:~~

(i) a compound of formula (I)



or a pharmaceutically acceptable salt, ester, or solvate of the compound, wherein:

*B3  
W.M.*  
n is 1-3;

X is either O or S;

~~R<sub>1</sub> R<sup>1</sup> is selected from the group consisting of C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or alkenyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, aryl, heteroaryl, carbocycle, or heterocycle;~~

D is a bond, ~~or a~~ C<sub>1</sub>-C<sub>10</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>10</sub> alkenyl or C<sub>2</sub>-C<sub>10</sub> alkynyl;

~~R<sub>2</sub> R<sup>2</sup> is carboxylic acid or a carboxylic acid isostere;~~

~~and wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is optionally substituted with one or more substituents selected from R<sup>3</sup>, where R<sup>3</sup> is hydrogen, hydroxy, halo, haloalkyl, thiocarbonyl, alkoxy, alenoxy, alkylaryloxy, aryloxy, arylalkyloxy, cyano, nitro, imino, alkylamino, aminoalkyl, sulphydryl, thioalkyl, alkylthio, sulfonyl, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl or alkynyl, aryl, aralkyl, heteroaryl, carbocycle, heterocycle, and CO<sub>2</sub>R<sup>7</sup> wherein R<sup>7</sup> is hydrogen, or C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl; and~~

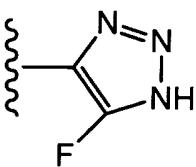
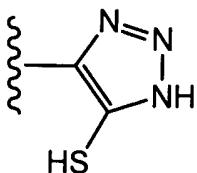
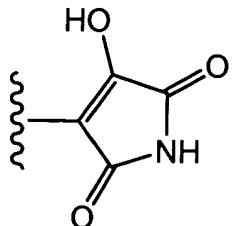
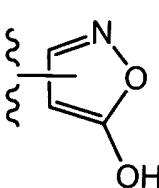
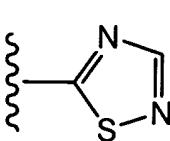
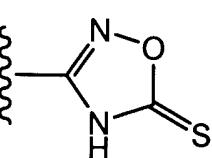
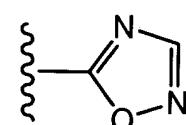
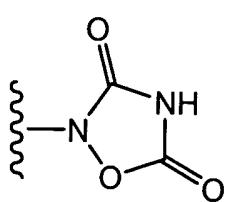
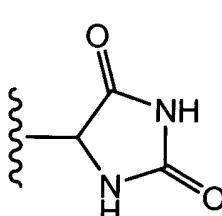
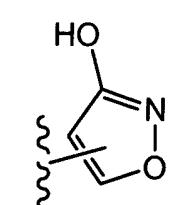
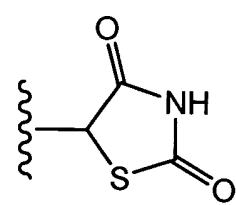
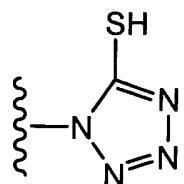
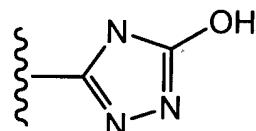
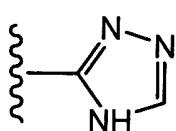
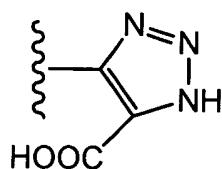
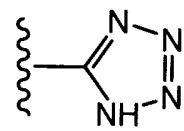
~~or a pharmaceutically acceptable salt, ester, or solvate thereof~~

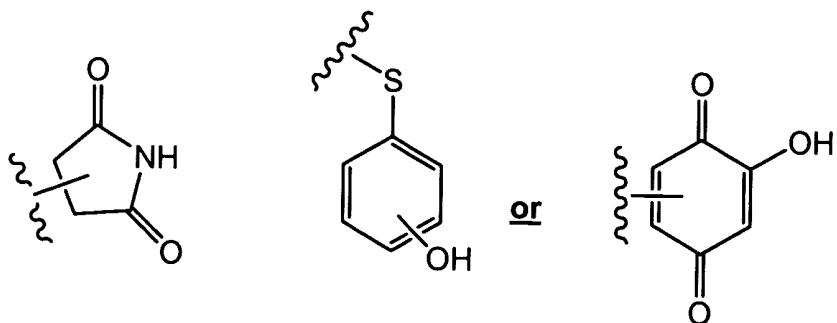
(ii) a pharmaceutically acceptable carrier.

Claim 10 (currently amended): The pharmaceutical composition of claim 9, wherein  $\underline{R_2 R^2}$  is a carbocycle or heterocycle containing any combination of CH<sub>2</sub>, O, S, or N in any chemically stable oxidation state, wherein any of the atoms of said ring structure are is optionally substituted in one or more positions with R<sup>3</sup>.

Claim 11 (currently amended): The pharmaceutical composition of claim 9, wherein  $\underline{R_2 R^2}$  is ~~selected from the following group:~~

*B<sup>3</sup>*  
*cont.*





B3  
cont.

wherein the atoms of said ring structure may be is optionally substituted at one or more positions with R<sup>3</sup>.

Claim 12 (canceled)

Claim 13 (currently amended): The pharmaceutical composition of claim 9, wherein the ~~N-heterocyclic carboxylic acid or carboxylic acid isostere~~ compound is selected from the group consisting of compounds 1-139 1, 3, 5, 8, 11, 14, 17, 21, 24-32, 34, 38-40, 44, 45, 47-52, 62, 64-68, 73-98, 101, 102, 106, 108-117 and 119- 137 of Tables I, II and III.

B4  
Claims 14-82 (canceled)